REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 1, 3-7, 9, 12-17, 21-30, 32, 33, 35-39, 43, 44, 51-62 presently appear in this application, with claims 24-29, 51-58, 60 and 61 withdrawn from consideration by the examiner, define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 15, 21-23, 30 and 43-45 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement for an intended use for treating or inhibiting the development of colon cancer with the inventive MHC-class I binding, CTL-inducing peptides presented as a "cell composition". The examiner states that applicants are required to show with a reasonable number of examples that the peptide(s) in fact could be presented by a APC in order to accomplish the required elicitation of a CTL response. This rejection is respectfully traversed.

Page 1658, right column, first full paragraph, of the Tirosh et al., *British J. Cancer* 97:1655-1663, that is part of the declaration attached hereto and which corresponds to the results in Example 1, paragraphs [00111]-00112] on pages 46-48, teaches that 503 peptides from proteins encoded by 26 genes overexpressed at least five fold in colon tumor tissues were

loaded onto ^{35}S-labelled RMA-S/HHD/B7.1 cells to serve as targets for CTL. Targets that were specifically lysed by more than 10% over the negative control in two consecutive experiments were regarded as a positive hit (target of CTLs). Table 2 of Tirosh et al. and Table 3 of the present specification show a list of twenty two antigenic peptides which were then tested *in vivo* and seven were considered to elicit a CTL response (see Fig. 2A of Tirosh and Fig. 4 of the instant application). Accordingly, the seven antigenic peptides from five different proteins overexpressed in colon tumor tissue provide a reasonable number of examples to satisfy the enablement requirement.

Insofar as this enablement rejection is concerned, there are many examples in the prior art that the loading technique used in present specification and in the Tirosh et al. paper submitted with the attached declaration is one way to get peptides presented by APCs. The present inventors did not invent anything with respect to such techniques; they just used it to for loading antigenic peptides. However, one of ordinary skill in the art would expect that if peptides can be presented by APCs using the loading technique(s) mentioned in the present specification, then one of ordinary skill in the art would also expect that they would also be presented using genetic engineering techniques known in the art.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 3, 4, 9, 12-17, 21-23, 30-33, 35-39, 43-45 and 62 have been rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for a peptide isolated from a protein expressed by any polynucleotide from a human colon carcinoma cell where the peptide has the ability to bind MHC Class I and elicit a peptide-specific CTL response and where the peptide optionally includes at least one non-natural modification. The examiner contends that applicants' own data in the specification are dispositive to the assertion that not just any peptide can be designed that would predictably bind MHC to promote a CTL response *in vitro* much less *in vivo*. This rejection is respectfully traversed.

Applicants respectfully disagree with the examiner's position. First, applicants' own data in Example 1, paragraphs [00111]-[00113] on pages 46-50 of the present specification and in Tirosh et al., page 1658, right column, show that of 503 HLA-A2.1-restricted peptides (from 26 genes tested so far), 22 bind MHC and are targets for CTLs and seven were considered to elicit a CTL response *in vivo*. Obtaining seven peptides that elicit a CTL response from 503 potential candidates from 26 overexpressed proteins is not a rare occurrence. If more genes overexpressed in colon tumor cells are screened or if peptides from the 26

overexpressed proteins restricted to other HLA class I molecules are screened as targets for CTLs, as was done with HLA-A2.1-restricted peptides in the present specification and in Tirosh et al., then more TAA peptides that elicit a CTL response would be expected to be identified with routine experimentation.

It is well within the skill of those in the art based on the guidance provided in the present specification to screen peptides for binding to MHC. Peptides that do not bind are not within the scope of the claims. It does not matter how many peptides the applicants have that are operable or not operable because this can be readily determined in a routine screen. The screen is first a simple binding assay of a peptide to MHC and then a determination if the MHC presenting the peptide will elicit a CTL response. One of ordinary skill in the art would well recognize and understand how to go about conducting this screening with only routine experimentation based on the guidance provided in the present specification. The Federal Circuit Court of Appeals held in *In re Wands* 8 USPQ2d 1406, 1407 that:

> Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes a desired antibody… However, it seems unlikely that undue experimentation would be defined in terms of the number of hybridomas that were never screened.

The examiner has invited applicants to resubmit the new data in the form of a 1.132 Declaration signed by one of the inventors.

Attached hereto is a 1.132 Declaration executed by Lea Eisenbach, one of the inventors, which presents the new data as an attached unpublished report. In the "Summary" of the report, it is disclosed that four variants of peptide 3-7 and eight variants of peptide 3-5 were synthesized and their binding to HLA-A2.1 was determined by an MHC class I stabilization assay. It was found that all the variants of peptide 3-7 bind to HLA-A2.1 and that in variants of peptide 3-5, substitution of isoleucine (I) by asparagine (N) reduced the binding to HLA while other substitutions did not affect binding. General guidance for amino acid substitutions are provided in the present specification on pages 30-32, paragraphs [0062]-[0068].

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 5, 6 and 59 have been rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for any immunogenic peptide derived from the protein encoded by the nucleotide sequence of SEQ ID NO:58 or SEQ ID NO:60. This rejection is respectfully traversed.

As argued immediately above in the enablement rejection of claims 1, 3, 4, 9, 12-17, 21-23, 30-33, 35-39, 43-45 and 62,

one of ordinary skill in the art would be fully enabled for identifying TAA peptides from human 1-8D interferon inducible protein 2 and a polymorphism thereof by following the guidance provided in the present specification for the 1-8D protein, where peptides identified as HLA-A2.1-restricted were tested as targets for CTLs *in vitro* and for eliciting a CTL response *in vivo*. There is no undue experimentation, as one of ordinary skill in the art could easily follow what was done with 1-8D with only routine experimentation to obtain from the 1-8D interferon inducible protein 2, or a polymorphism thereof, the TAA peptide presently claimed.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 3-7, 9, 12-17, 21-23 and 62 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The examiner states that applicants have not and cannot identify *per se* support in the specification for the negative limitation "is not a six transmembrane epithelial antigen of the prostate (STEAP) protein" as presently recited. This rejection is respectfully traversed.

As stated in MPEP 2173.01:

> A fundamental principle contained in **35 U.S.C. 112**, second paragraph is that applicants are their own lexicographers. They

> can define in the claims what they regard as their invention essentially in whatever terms they choose so long as **>any special meaning assigned to a term is clearly set forth in the specification. See MPEP § **2111.01.**< Applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the court in *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought. (emphasis added)

MPEP 2173.05(i) on Negative Limitations further states:

> The current view of the courts is that there is nothing inherently ambiguous or uncertain about a negative limitation. So long as the boundaries of the patent protection sought are set forth definitely, albeit negatively, the claim complies with the requirements of **35 U.S.C. 112**, second paragraph. Some older cases were critical of negative limitations because they tended to define the invention in terms of what it was not, rather than pointing out the invention. Thus, the court observed that the limitation "R is an alkenyl radical other than 2-butenyl and 2,4-pentadienyl" was a negative limitation that rendered the claim indefinite because it was an attempt to claim the invention by excluding what the inventors did not invent rather than distinctly and particularly pointing out what they did invent. *In re Schechter*, 205 F.2d 185, 98 USPQ 144 (CCPA 1953).
>
> A claim which recited the limitation "said homopolymer being free from the proteins, soaps, resins, and sugars present in natural Hevea rubber" in order to exclude the characteristics of the prior art product, was considered definite because each recited limitation was definite. *In re Wakefield*, 422

> F.2d 897, 899, 904, 164 USPQ 636, 638, 641 (CCPA 1970). In addition, the court found that the negative limitation "incapable of forming a dye with said oxidized developing agent" was definite because the boundaries of the patent protection sought were clear. *In re Barr*, 444 F.2d 588, 170 USPQ 330 (CCPA 1971).
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> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). (emphasis added)

The decision in *In re Johnson* 194 USPQ 196 (CCPA 1977), which is what is currently accepted by the courts and the USPTO, states:

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. All that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count.
>
> The board indicated that "it is manifestly immaterial" *why* appellants limited their claims. Though it is true that insufficiency under §112 could not be cured by citing the

> causes for such insufficiency, it is not true that the factual context out of which the question under §112 arises is immaterial. Quite the contrary. Here, as we hold on the facts of this case, the "written description" in the 1963 specification supported the claims in the absence of the limitation, and that specification, having described the whole, necessarily described the part remaining. The facts of the prosecution are properly presented and relied on, under these circumstances, to indicate that appellants are merely excising the invention of another, to which they are not entitled, and are not creating an "artificial subgenus" or claiming "new matter." (emphasis added)

In short, the positive recitation in the present specification of STEAP indeed provides adequate written description to excise what applicants are not entitled to from their claimed invention by the use of negative limitations. Such negative limitations, which have basis in the original disclosure only as positive recitations, are permitted.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 30-32 have been rejected under 35 U.S.C. §102(e) as being anticipated by Matsuzaki et al., US20030092037. This rejection is obviated by the cancellation of claim 31 and the amendment to claim 30 to delete the recitation of the full length TAA encoded by the 1-8D interferon inducible gene. Claims 30, 32 and 33, as amended, do not read on a full length TAA, e.g., of SEQ ID NO:59, and cannot be anticipated by Matsuzaki.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 30 and 31 have been rejected under 35 U.S.C. §102(e) as being anticipated by Berger et al., US20030148410. This rejection is also obviated by the cancellation of claim 31 and the amendment to claim 30 to delete the recitation of the full length TAA encoded by the human 1-8D interferon inducible gene.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting its allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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